

**REMARKS**

Upon entry of the above amendment, claims 65-69 and 71-78 will be pending in this application. Claim 68 has been amended for clarification. Claim 70 is cancelled without prejudice. New claims 72-78 are fully supported by the specification. For example, claims 72-74 are supported by page 16, lns. 13-27 and page 18, lns. 22-29; claims 75-77 are supported by original claim 1 and page 15, lns. 8-21; claim 78 is supported by original claim 7.

As a preliminary matter, Applicants have fully complied with the requirements for an amendment under 37 C.F.R. §1.121, by identifying in the Listing of Claims section that claims 1-64 are cancelled.

Further, Applicants acknowledge and thank the Office for the allowance of claims 65, 66 and 67.

**The Claims Are Enabled**

Claims 68, 69 and 71 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly being non-enabling. Specifically, the Office Action alleges that one of ordinary skill in the art would not know how to add only a “part” of a leucine based motif to a botulinum toxin that would increase the half-life of the botulinum toxin. Applicants respectfully disagree.

Applicants respectfully assert that claim 68, 69 and 71 are fully enabled by the specification. That is, one of ordinary skill would know how to add a part of a leucine based motif (a sequence of seven amino acids) to produce a botulinum toxin with an increased half-life. For example, a part of a leucine based motif is a sequence of amino acids less than seven amino acids, e.g., a sequence of six or two amino acids. The specification teaches that a leucine based motif comprises a “quintet of amino acid” and a “duplet of amino acids” to form a sequence of seven amino acids. Specification, page 16,

Ins. 29-34. Additionally, the specification teaches that the quintet of amino acids comprises, for example, E (glutamic acid) at the second position, and the duplet of amino acids comprises at least one hydrophobic amino acid, for example a leucine. As such, from reading the specification, one of ordinary skill would be enabled to make a sequence of six amino acids comprising, for example, a glutamic acid at the second position and a leucine at the sixth position. Also, one of ordinary skill can make a sequence of two amino acids comprising, for example, a duplet of amino acids. Moreover, one of ordinary skill may rely on the current state of recombinant technology to conduct **routine** experiments to arrive at other sequences that are parts of the leucine based motif, wherein these parts may be used in accordance with claims 68, 69 and 71. Accordingly, these claims are enabled.

#### **The Claims Are Definite**

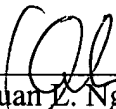
Claims 68, 69 and 71 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Particularly, the Office Action alleges that “It is ambiguous whether an ‘additional’ leucine based motif ‘is added’ to the claimed BoTN molecule, which alternatively still contains its naturally-occurring leucine based motif.” For clarification, claim 68 has been amended to recite that the leucine based motif of SEQ ID NO: 2 is added to the toxin in addition to the naturally-occurring leucine based motif. Further, new claim 75 has been added to recite that the naturally-occurring leucine based motif of the toxin is substituted by SEQ ID NO: 2, wherein SEQ ID NO: 2 is not the same as the naturally-occurring leucine based motif.

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**PATENT**

In view of the foregoing, Applicants submit that the pending claims are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,

  
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